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US study shows an increased risk of dementia in men ageing with HIV

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Do men who age with HIV have a higher risk of dementia than their HIV-negative counterparts? It may well be the case, according to a recent study conducted in the US by Dr Kirsten Bobrow, University of California San Francisco.

Like the general population, people with HIV experience multiple co-morbidities and age-associated diseases as they get older. Also, it has been demonstrated that once HIV enters the brain, as early as the first days of infection, it causes mild cognitive changes, which persist despite successful control of the virus with antiretroviral therapy (ART). Additionally, some anti-HIV drugs can themselves increase the risk of cerebrovascular, cardiovascular and metabolic diseases, which are known to affect brain health and increase the risk of dementia.

Published in *AIDS*, the study explored whether HIV is associated with a first diagnosis of dementia in older US veterans (former military personnel). To this

effect, the investigators used retrospective data collected in the US Veterans Health Administration System from 2005 to 2015. They included 1114 veterans living with HIV, aged at least 55 years and, for comparison, another group of 1114 HIV-negative veterans that was matched on age, sex, race, and substance use (drug abuse, alcohol abuse, tobacco use).

Glossary

Participants' records were reviewed, looking for incident dementia during a period that lasted until a first dementia diagnosis, death or the end of the study. Dementia of any cause was included, including HIV-associated dementia, Alzheimer's disease and vascular dementia. However, prion disease dementia and dementia caused by alcohol or drug abuse were excluded.

Demographics at baseline

In the cohort of 2228 veterans, mean age was 62.5 years at entry in the study (baseline). Over 98% of participants were male; 52% were non-Hispanic White, 38% non-Hispanic Black and 10% other.

At baseline, health risk behaviours and noncommunicable diseases were common in the cohort. Twenty-two per cent of participants had a history of tobacco use, while about 18% had been diagnosed with alcohol/drug abuse. Moreover, 17% of participants had diabetes, 34% had a high blood pressure and 7% a history of stroke or transient ischaemic attack (mini-stroke).

Generally speaking, the comparison groups were well-matched in terms of individual variables. However, the baseline rate of depression was significantly higher among veterans with HIV, who were also more likely to be better educated but tended to have a lower income.

Results: incident dementia

During the follow-up period of up to eleven years (mean five years), 57 cases of incident dementia (5.1%) were diagnosed among veterans with HIV, compared with 33 among their HIV-negative counterparts (3%). The type of dementia was unspecified in two-thirds of cases.

Out of the 57 cases affecting veterans with HIV, eleven (19%) were HIV-associated dementia (HAD). Apart from HAD, the patterns of dementia subtypes, where recorded, were somewhat similar in both groups: four Alzheimer's disease (7%) and six vascular dementia (10%) in veterans with

HIV, compared with four Alzheimer's disease (10%), six vascular dementia (18%) and two frontotemporal dementia (caused by uncommon brain disorders that affect the frontal and temporal lobes of the brain) in HIV-negative veterans.

After accounting for the competing risk of death and adjusting for age, sex, race/ethnicity, substance use, education and income, veterans with HIV still had a 50% higher chance of being diagnosed with dementia (hazard ratio 1.50, 95% CI 0.96-2.35) than their HIV-negative counterparts.

In terms of cumulative incidence, around 20% of veterans with HIV would be expected to be diagnosed with dementia by the age of 70, whereas in those without HIV, 20% would receive this diagnosis by age 76.

Results: risk factors

Only 61% of veterans with HIV received ART, and those who did had lower CD4 counts, fewer medical visits, longer follow-up time and worse risk factors:

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- Diabetes: 15.9% in those not on ART vs 18.7% in those on ART.
- Depression: 18.4% vs 26.2%.
- Drug/alcohol abuse: 14.7% vs 21.8%.
- Average CD4 cell count: 539 vs 481.

Veterans who took ART had a significantly higher risk of being diagnosed with dementia (adjusted Hazard Ratio 1.78, 95% CI 1.11-2.85), compared with those not taking ART and HIV-negative veterans. However, when these results were adjusted for CD4 cell count, the differences were no longer significant (aHR 1.20, 95% CI 0.50-2.86).

As for the different types of antiretroviral regimens, there was no convincing evidence that any had more or less of an effect on risk estimates than the other.

Conclusion

As clearly highlighted by the authors, the main result from this research is that HIV was associated with an increased risk of dementia diagnosis during follow-up.

Veterans with had higher of being diagnosed with dementia than their negative counterparts

Less clear is the increased risk associated with ART. It may be driven by differences in virologic control – measured indirectly, through CD4 counts – and other health differences, which may have an effect similar to that of other known risk factors for dementia. Importantly, the group on ART had lower CD4 nadirs and presented with lower CD4 counts at the time of dementia diagnosis. It was probably the sickest veterans who were prescribed ART.

What makes this study particularly interesting is that much of previous research exploring the risk of dementia in people with HIV have focused on the risks of HIV-associated dementia (HAD), although this condition is less common in the era of widely available ART. Without minimising the role of HAD, the investigators also explored HIV “on its own” as a potential risk factor for other types of dementia. Not only did they find that HIV is associated with an increased risk of incident dementia, but also that differences in risks associated with the ART were driven by differences in disease severity.

By which mechanisms does this increased risk occur? So far, they are not understood. This brings Bobrow and colleagues to conclude: “It is critical to understand the mechanisms by which risk is increased (particularly dementia subtypes), whether biological or socially patterned”.

References

Bobrow K et al. *HIV and risk of dementia in older veterans*. AIDS 34: 1673-1679, 2020. doi: 10.1097/QAD.0000000000002597